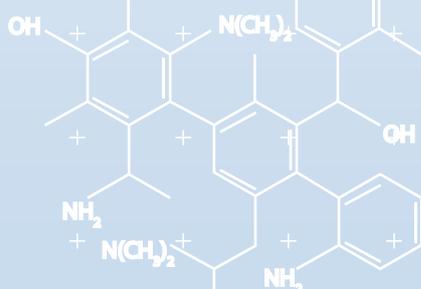


Fast Track to Metabolic Biomarker Signatures: **Absolute/DQ[®] p180 Kit**



**Targeted Metabolomics
Designed for Clinical Utility**



The Fast and Reproducible Way to Targeted Metabolomics Results

The Absolute*IDQ*® p180 Kit quantifies a broad metabolite spectrum, reflecting diverse **pathophysiological processes** such as inflammation, mitochondrial dysfunction, or cell cycle control. In hundreds of research projects, the kit has provided circulatory biomarker signatures for diagnosis, prognosis or prediction in multi-factorial diseases.

This **standardized** solution is designed to support targeted metabolomics studies in large-scale **epidemiological and clinical cohorts**. It is ideal for research projects where long-term reliability and throughput matter. The minimal sample volume needed enables longitudinal analyses in small animal models.



Why Metabolomics? Why Choose a Targeted Approach?

The metabolome integrates an individual's genetic background, aging, lifestyle and environmental factors. As it closely **reflects the phenotype**, the metabolome can provide important information about the state of a cell, organ, or organism. Most metabolic pathways are identical in humans and animal models, also making metabolomics ideally suited for **translational research** approaches.

The biochemical diversity of metabolic substances makes it impossible to cover the full metabolome with a single analytical method - **targeted coverage of carefully selected pathways** is the **key to successful metabolomics projects**. Focusing on pre-defined analytes allows identifying and quantifying challenging metabolites confidently.

Covered Metabolite Classes and Relevance in Main Application Areas

The **up to 188 analytes** covered by the Absolute*IDQ*® p180 Kit span four main areas: amino acid (21 amino acids and 21 biogenic amines), glucose (sum of hexoses), fatty acid (40 acylcarnitines) and lipid metabolism (90 glycerophospholipids and 15 sphingolipids). Those

reflect a vast number of biological functions and rate limiting enzymes. The table below exemplifies the relevance of selected metabolites **in main application areas**.

Metabolites/ Indication	Amino Acids and Biogenic Amines	Acylcarnitines	Glycerophospho- and Sphingolipids	Hexoses
Oncology	Serine: link between glycolysis, lipid and nucleotide metabolism Leucine, arginine: mTOR activation	Tumor metabolism: increased usage of fatty acids as nutrients	Growth and proliferation: lipids required as building blocks Cancer risk: lipid metabolism modulates probability of future disease	Glycolysis: strongly upregulated in many cancers
Cardiology	Phenylalanine to tyrosine ratio: marker for endothelial function NO signaling: involved in angiogenesis and cardiomyocyte homeostasis	Cardiomyocytes: fatty acid oxidation is the main source of energy	Atherosclerotic plaque inflammation: lipid breakdown by PLA2 involved	Insulin resistance: major risk factor for cardiovascular disease
Diabetes	Branched chain amino acids: involved in insulin resistance Tryptophan, kynurenine: role of immune pathways in diabetes	Mitochondrial function: affects inflammation and lipid accumulation in the liver	Lipoproteins: Metformin alters LDL cholesterol levels via lipid metabolism Low-grade inflammation: lipids are inflammatory mediators	Disturbed glucose homeostasis: major hallmark
Neurology	Neurotransmitter function: e.g. glutamate, dopamine, serotonin Urea cycle deregulation: probable involvement in neurodegeneration	Neurodegeneration: evidence for involvement of mitochondrial metabolism	Myelin sheaths: sphingolipids are a major component	Insulin resistance: contributes to development of Alzheimer's disease

Table: Indications and relevant metabolites (relevant literature available upon request)



Key Benefits

- **Comprehensive information** about the physiological state of an organism
 - Broad analyte coverage of up to 188 metabolites
- **Highly reproducible** due to standardization and quality control
 - Proven in a multinational ring trial
- **Quantitative** - easy to handle data format
- **High throughput** (up to 500 samples per week)
- Saving precious sample material
 - **Only 10 µL** needed for most biofluids, fully validated for human plasma
 - Strong experience with **many biological matrices**
- **Ready to use** - no method development required



Standardization, Throughput and Proven Reproducibility

Building upon previous studies is drastically simplified by reproducibility of analytical procedures, and the possibility to acquire data quickly.

The AbsoluteDQ® p180 Kit is a **widely used** targeted metabolomics solution. Having proven inter-platform, inter-laboratory reproducibility and providing high throughput, it can significantly **increase research output and confidence** in the findings.

The AbsoluteDQ® p180 Kit has been used in hundreds of metabolomics projects, spanning all major fields of healthcare spending. We will be happy to inform you about available results from research questions related to yours.

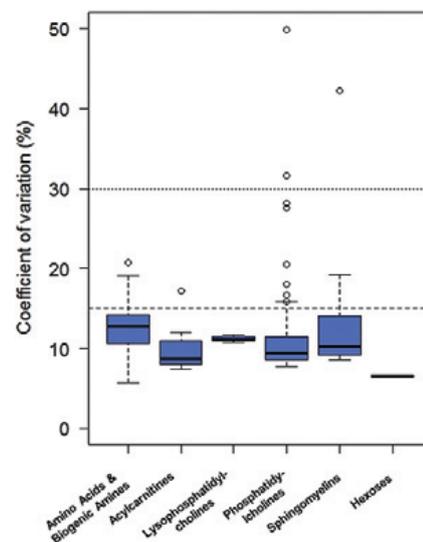


Figure: Inter-platform reproducibility of the AbsoluteDQ® p180 Kit (internal reproducibility data; unpublished)

How to Generate Data

The AbsoluteDQ® p180 Kit relies on triple quadrupole mass spectrometry – a technology that is in routine clinical use, for example in newborn screening, pharmacology and toxicol-

ogy. The table below shows different options how data can be generated. Contact us to discuss how to move forward.

Use of Kits in Your Laboratory	Collaboration	Metabolic Phenotyping Services
<ul style="list-style-type: none"> • You have a suitable mass spectrometer. • Biocrates provides the kit with validated method, reagents, and required software. Contact us for a detailed list of requirements.	<ul style="list-style-type: none"> • You intend to do measurements through a partner laboratory. • Biocrates can provide kits and technical support directly to your collaborator. We will be pleased to connect you with potential partners.	<ul style="list-style-type: none"> • The full analytical workflow is performed at Biocrates' laboratories. • Biocrates ensures short turnaround times and can provide biostatistical support. Contact us for further information.

Workflow (for measurement in your own laboratory)

Sample Preparation (3-5 hours)

First Steps

Samples are registered in the Met*IDQ*® software (provided with the kit). The testmix is used to ensure suitable system conditions.

Loading

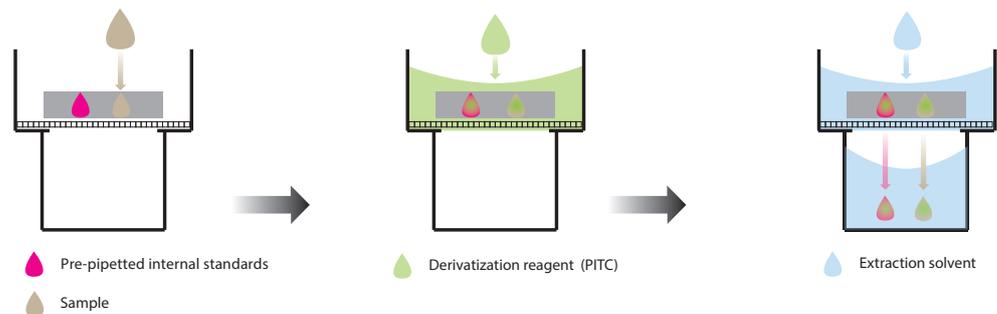
Samples and reagents are loaded onto the plate. See plate layout for further details.

Derivatization

Analyzing biogenic amines and amino acids reliably requires derivatization.

Extraction

Metabolites are extracted with organic solvent, for subsequent mass spectrometric analysis in two steps.



Sample Processing (24-34 hours)*

Run Samples

First, the liquid chromatography (LC-MS) part for amino acids and biogenic amines is run, followed by the flow injection (FIA-MS) part for all other metabolites.

Quantify

Quantitative LC-MS data is imported into the Met*IDQ*® software, FIA-MS data is quantified by Biocrates' software.

Quality Control

Met*IDQ*® performs an automated quality assessment. Additional manual checks can be made.

Statistics and Export

Met*IDQ*® supports basic statistics, as well as export of data. Upgrades for Met*IDQ*® are available, enabling extended data analysis within the software package.

* Depending on analytical platform

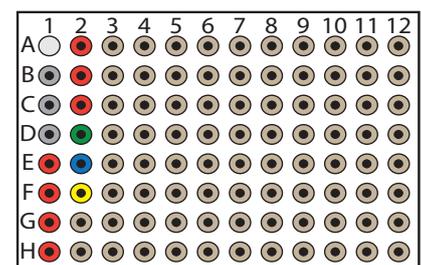
** minimum time for quality control and export of data

Plate Layout

The Absolute*IDQ*® p180 Kit comes in a convenient 96 well format, for the measurement of up to 82 samples.

A minimum of 16 wells per plate is reserved for zero sample, 3 blank samples, 7 calibration standard levels (for amino acids and biogenic amines), and a minimum of 3 quality control samples. These quality assurance provisions, together with a patented plate design, are major contributors to analytical precision and reproducibility.

- Blank; no sample, no ISTD
- Zero sample; no sample but ISTD
- Samples
- ISTD
- 7 point calibrator standards for LC-MS/MS part
- Quality controls (QC) in low, medium, high concentration



The Absolute*IDQ*® p180 Kit: Fast Track to Metabolic Biomarker Signatures!

Products

Product Description	Product Number
Absolute <i>IDQ</i> ® p180 Kit - (96)	Contact us
Met <i>IDQ</i> ™ StatPack Module	9120052120189
Met <i>IDQ</i> ™ Ratio Explorer Module	9120052120899

If you want to learn more, contact us!

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The Absolute*IDQ*® p180 Kit is designed for research use only.
Not for in-vitro diagnostic use